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Trials

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Investigating the effectiveness and cost-effectiveness of FITNET-NHS (Fatigue In Teenagers on the interNET in the NHS) compared to activity management to treat paediatric chronic fatigue syndrome (CFS)/ myalgic encephalomyelitis (ME): amendment to the published protocol

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Abstract

The FITNET-NHS Trial is a UK, national, trial investigating whether an online cognitive behavioural therapy program (FITNET-NHS) for treating chronic fatigue syndrome/ME in adolescents is clinically effective and cost-effective in the NHS. At the time of writing (September 2019), the trial was recruiting participants. This article presents an update to the planned sample size and data collection duration previously published within the trial protocol.

Trial registration: ISRCTN, ID: 18020851. Registered 8 April 2016.

Keywords: Paediatrics, Chronic fatigue syndrome, Myalgic encephalomyelitis, CFS/ME, CBT, Online systems, E-therapy, Methodology, Recruitment, Trial

Background

The FITNET-NHS Trial is a United Kingdom (UK), national ,randomised controlled trial testing the acceptability, effectiveness and cost-effectiveness of an online cognitive behavioural therapy (CBT) programme, FITNET-NHS (Fatigue In Teenagers on the interNET in the National Health Service), designed to treat adolescents with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) [1]. In the UK, most young people with CFS/ME do not have access to local NHS specialist medical care for the condition, as there are limited paediatric CFS/ME specialist centres in the UK. The FITNET-NHS trial was set up to test the *online delivery* of specialist care from one specialist paediatric CFS/ME site in the south west of England as a means of addressing this problem. Recruitment projections were estimated in advance and were based on reaching national paediatric CFS/ME populations at high volumes – made possible due to our innovative methodology using entirely remote processes for recruitment and treatment delivery. The original sample size target if achieved would have given us sufficient statistical power to detect a true effect of FITNET-NHS within the subgroup of participants with co-morbid mood disorder.

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The current article is an amendment to our previously published protocol for the FITNET-NHS Trial: Baos et al. (2018) [1].

Amendment

Recruitment into the FITNET-NHS Trial began on 1 November 2016. In mid-2018, it became apparent that the recruitment rate would not allow us to achieve our original sample size target ($n = 734$) without a substantial extension to the recruitment period. The original sample size was selected to provide 80% power to detect a 0.4-standard deviation (SD) difference at 5% significance with 10% attrition on the primary outcome in a *subgroup* of participants (estimated to be 30% or $n = 220$) with co-morbid mood disorders of anxiety and depression. For all participants (with or without co-morbid mood disorders), the original sample size provided 97% power at 1% significance to detect a 0.35-SD difference on the primary outcome (Short Form Health Survey; Physical function Subscale (SF-36-PFS) score) at 6 months.

We reviewed the trial with the funders – National Institute for Health Research, Health Technology Assessment (NIHR HTA, on 10 July 2018) and consulted with the Trial Management Group (TMG, on 12 September 2018 and 18 October 2018), the Data Safety Monitoring Committee (DSMC, on 10 October 2018 and by email report on 11 March 2019) and the Trial Steering Committee (TSC, on 28 November 2018).

In September 2018, we calculated the required sample size for the primary outcome in all participants (with or without co-morbid mood disorders):

Data on 266 children will give us 90% power at 5% significance to detect a 0.4-SD difference on the SF-36-PFS. With attrition currently at approximately 15%, we will need to recruit 314 children. This is achievable (based on recruitment rates to date) by the end of October 2020.

This gave us a new recruitment target of 314 children in total, 157 in each treatment group

We considered the issue of co-morbid disorders. On 2 October 2018, we investigated the rate of co-morbid mood disorders in FITNET-NHS participants at baseline. This was higher than our original estimates as the rate of co-morbid mood disorders was 40% (compared to 30% in our original estimates). With the revised sample size target of 314 there will be approximately 106 participants with co-morbid mood disorders (53 in each treatment group). This will give 53% power at 5% significance to detect a 0.4-SD difference on the SF-36-PFS between treatment groups within this co-morbid subgroup.

From consultation with the NIHR HTA, TSC, DSMC and TMG, the decision was made to agree revised recruitment targets and extend the recruitment time by 6 months to enable the FITNET-NHS Trial to achieve the primary aim of testing the effectiveness (and cost-effectiveness) of the FITNET-NHS treatment compared to Activity Management. The NIHR HTA gave their approval in principle of this change on 30 January 2019, subsequent to provision of documentation. Full NIHR HTA approval for revised recruitment target and the contract variation to include the 6-month extension to the project timeline was received on 24 April 2019. We will, therefore, recruit 314 children and recruitment will finish on 31 October 2020. Follow up will finish on 31 October 2021.

We have followed standard procedures to update all relevant organisations regarding these changes, including trial registration (ISRCTN, ID: 18020851: change accepted and records updated on 1 July 2019), and submitting as a substantial trial amendment to the Research Ethics Committee (REC, approved on 26 July 2019) and the Health Research Authority (HRA, approved on 10 July 2019).

With our revised recruitment target of 314 participants, the FITNET-NHS is still set to be the largest paediatric CFS/ME treatment trial in the UK and globally, the results of which will should the future of paediatric CFS/ME treatment delivery.

Abbreviations

CBT: Cognitive behavioural therapy; CFS/ME: Chronic fatigue syndrome/myalgic encephalomyelitis; DSMC: Data Safety and Monitoring Committee; FITNET-NHS: Fatigue In Teenagers on the interNET in the NHS; HRA: Health Research Authority; ISRCTN: International Standard Randomised Controlled Trials Number; NIHR HTA: National Institute for Health Research, Health Technology Assessment; REC: Research Ethics Committee; SD: Standard deviation; SF-36-PFS: Short Form Health Survey (36 question): Physical Function Subscale; TMG: Trial Management Group; TSC: Trial Steering Committee; UK: United Kingdom

Acknowledgements

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Authors' contributions

EC: trial conception, chief investigator, reviewing of manuscript. EA: oversight of the trial as part of the TMG, trial manager, drafting and reviewing of manuscript. MR: oversight of the trial as part of TMG, trial research associate, manuscript review. WH: oversight of the trial as part of the TMG, lead on health economics, manuscript review. NM: oversight of the trial as part of the TMG, lead on qualitative methods, manuscript review. LB: oversight of the trial as part of the TMG, qualitative researcher, manuscript review. DG: trial statistician, confidential reporting to the Data Monitoring Committee, manuscript drafting and review. CM: oversight of the trial as part of the TMG,

statistical lead, manuscript drafting and review. RP: oversight of the trial as part of the TMG, qualitative researcher, manuscript review. DK: oversight of the trial as part of the TMG, lead on recruitment from primary care, manuscript review. JM: oversight of the trial as part of the TMG, lead on data linkage, manuscript review. PS: oversight of the trial as part of the TMG, clinical psychology support, manuscript review. HK: oversight of the trial as part of the TMG, lead clinical psychologist, trained and supervised therapists, manuscript review. EVP: oversight of the trial as part of the TMG, FITNET advisor, manuscript review. SN: oversight of the trial as part of the TMG, FITNET advisor, manuscript review. GB: oversight of the trial as part of the TMG, FITNET advisor, manuscript review. All authors read and approved the final manuscript.

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Availability of data and materials
The research staff will have access to the de-identified data during the project period, and 5 years following the completion of the trial for contributing to knowledge building through dissemination of research reports.

Ethics approval and consent to participate
The RCT protocol has been reviewed and approved by the South West – Frenchay Research Ethics Committee (16/SW/0268). Both the young person and their caregiver need to give consent/assent. Amendments to the trial protocol are approved by the sponsor (and the Research Ethics Committee if appropriate) prior to implementation.

Consent for publication
Not applicable

Competing interests
EC is a medical advisor for the Sussex and Kent ME Society.
HK and GB received royalties for publication of treatment manual for CBT in CFS/ME in adults.
Other than those stated, above, the remaining authors have nothing to declare.

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